Remarks

Claims 1, 13, 15-16 and 17-36 have been canceled without prejudice. Claims 2-5, 7, 9, 11-12, 14 and 37 have been amended to more distinctly describe the claimed subject matter. Accordingly, claims 2-12, 14 and 37 are pending. Support for the amendments can be found throughout the specification and claims as originally filed. No new matter has been added.

Elections/Restrictions

The Examiner has rejected Applicant's arguments that the examination of all the claimed inventions would not present an undue burden. The Examiner states that the "arguments are not found persuasive because, although there may be an allowable linking concept, in the interim the Examiner would be forced to search each of the various claimed methods".

Applicants respectfully maintain their traversal.

As stated by Applicants in the interview, Applicants respectfully traverse the above stated restriction of the invention.

Applicants assert that the subject matter of Groups I-VII, claims 1-25, represent different embodiments of a single inventive concept which merit examination in a single application. More particularly, all the claims are linked by a single, searchable, unifying aspect; i.e., assays for the identification of antibiotics which feature the determination of an effect on a pantothenate kinase (e.g., CoaX), wherein said assays all utilize pantothenate kinase-based readout in their determination. Exemplary pantothenate kinase-based readouts include determining the ability of the compound to inhibit CoaX protein activity; determining the ability of the compound to bind CoaX; determining the ability of the compound to inhibit CoaX protein activity, and to bind CoaX; determining the ability of the compound to modulate the ability of pantothenate (or a pantothenate analog) to bind CoaX; and determining the compound's ability to modulate the kinase's activity in a cell expressing the kinase.

Applicants submit that the search and examination of claims 1-25 (and newly added claim 37) would have substantial overlap, as evidenced by the identical classification of the inventions of Groups I-VII by the Examiner. Thus, no serious burden would result from searching and examining all claims in the same application. As the M.P.E.P. states:

> If the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions.

M.P.E.P. § 803 (7th ed., Rel. 78A, March 1999).

To further illustrate this unity of invention, Applicants set forth newly added claim 37 which is generic to groups I-VII as set forth by the Examiner. Applicants submit that Groups I-VII should be reformed as a single group, the group also including new Claim 37. Applicants respectfully request that substantive examination proceed with respect to these claims.

In order to be fully responsive to the outstanding Office Action, Applicants hereby provisionally elect ***Group I, with traverse,*** which corresponds to claims 1-12, for prosecution on the merits. As Group I is subject to further restriction by the Examiner as to the CoaX protein amino acid sequence, Applicants further elect ***Group I6***, which corresponds to the amino acid sequence of SEQ ID NO: 2. As Group VII is subject to further restriction by the Examiner as to the microorganism, Applicants further elect ***Group VII2*** which corresponds to *Bacillus subtlis*. Regarding these further elections, Applicants request clarification as to whether the further restriction of Groups I and VII is a species election or is another restriction. If this is another restriction of the invention, Applicants traverse this restriction and argue that Groups I1-I33 and Groups VII1-VII2 represent patentably distinct species of the inventions of Groups I and VII, respectfully, and request reconsideration of this restriction.

Applicants further reserve the right to traverse this restriction to the remaining, non-elected inventions (Groups VIII-X) in future prosecution.

Sequence Listing

The Examiner states that the application fails to comply with 37 C.F.R. §1.821 (a)(1) and (a)(2) as the paper copy of the sequence listing filed March 20, 2001 contained duplicate sequence identification numbers. In response to the Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures mailed from the Patent Office on May 23, 2001, Applicants submitted (on October 23, 2001) a diskette containing the Substitute Sequence Listing in computer readable form as required by 37 C.F.R. §1.821 (e). The substitute sequence listing corrected the duplication in sequence identifier numbers. The diskette was unreadable by the USPTO. A replacement diskette was provided on March 28, 2002. Applicants submitted a Substitute Sequence Listing (paper copy and diskette) on September 15, 2003. The Examiner will note that the newly-provided paper copy shows that the duplication of sequence identifier numbers has been corrected.

Information Disclosure Statement

The Examiner states that the Information Disclosure statement submitted May 9, 2003 is in compliance with the provisions of 37 C.F.R. §1.97 and has been accepted.

Drawings

The Examiner has rejected the drawings of this application because "the sequence identification numbers associated with various bacterial proteins in Figure 6 do not appear to match the bacterial species given for those sequence identifiers in the sequence listing".

Applicants note that the "sequence identifiers" in the previous version of Figure 6, were not in fact sequence identifier numbers as required by 37 C.F.R. §1.821(c). They were simply the identifiers used by the program ClustalW to perform the alignment analysis. They have been deleted from Figure 6.

Rejection of Claim 37 Under 35 USC §112, First Paragraph

Claim 37 is rejected under 35 USC §112, first paragraph, "because the specification, while being enabling for methods of identifying antibiotics by identifying compounds that reduce the activity of pantothenate kinase, does not reasonably provide enablement for such methods by identifying compounds that either bind to (no affect on activity) or increase pantothenate kinase activity".

Applicants respectfully traverse the Examiner's objection. It is Applicant's position that antibiotic identification methods that feature assaying for readouts other than inhibition of pantothenate kinase activity are fully enabled by the instant specification. In particular, assays for compounds that bind pantothenate kinase can be practiced according to the teachings of the instant specification, and, for example, in the context of appropriate controls and/or parameters, would be useful for identification of antibiotics. However, in order to advance prosecution of the instant case, Applicants have amended claim 37 to assaying for an inhibition of pantothenate kinase activity.

In view of the foregoing claim amendment, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 37 under 35 USC §112, first paragraph.

Claims 37 and 1-14 are rejected under 35 USC §112, first paragraph, as not being enabled. The Examiner states that "while the Applicant has shown some somewhat conserved regions among some of the proteins, there is not clearly preserved sequence of motif that one in the art would recognize as potentially identifying a family of proteins, or at least a family that includes all of the identified sequences". The Examiner relies on the teachings of Skolnick, *et al.* and Bork, *et al.* and asserts that each describes the "uncertainty in predicting protein function from its structure" and that the art "does not recognize that sequence homology is sufficient for identifying the function of proteins". The Examiner further cites Scott, *et al.* as teaching an instance where there was "misidentification of protein function due to reliance on protein sequence homology".

Applicants respectfully traverse. Skolnick, *et al.* teach a novel, alternative approach to the "sequence-to-function approach" based on structural descriptors of protein function sites. Skolnick, *et al.* teach that it is ***desirable*** to have the structure of a protein so that the plethora of genomic sequence can be annotated, however they also clearly state that no "dry method" is sufficient. The authors conclude that "[t]he disadvantages [of this approach] are that one needs to have the proteins structure before a function can be assigned and that the approach is limited to those functions associated with proteins with at least one solved structure, so that a functional-site descriptor can be constructed". Furthermore, "[d]etailed descriptors will only work on the ***experimentally*** determined high-quality structures, and since no genome has the function of all proteins experimentally annotated, "it is impossible to know how many proteins with the specified biochemical function were not properly identified".

Bork teaches that each technology necessary for high-throughput research has its limits. Bork warns that the overwhelming amount of data stored in public databases is fraught with errors and leads to the errors in computational sequence analysis that he describes. In fact, Bork teaches that the use of complementary information may limit errors in function prediction, *e.g.,* since "function can be predicted by exploitation of genomic context", *e.g.,* conserved gene order. Bork concludes that "there is no doubt that sequence analysis is extremely powerful and that the generation of hypotheses derived by computational methods will be more often the first successful step in the design of experiments. If 70% of such experiments were successful, the speed of scientific discoveries would grow exponentially".

Scott, *et al.* teach the functional analysis of a previously identified gene, *PDS,* which when mutated is responsible for Pendred Syndrome. They state, "Pendrin is closely related to a family of sulfate transporter proteins....On the basis of this homology and the presence of a ***slightly modified*** sulfate-transporter signature sequence comprising its putative second transmembrane domain, pendrin has been ***proposed*** to function as a sulfate transporter". Based on their functional analyses, Scott, *et al.* conclude that pendrin functions as a chloride-iodide transport protein and not a sulfate transporter. Based on these results, Scott, *et al.* state "[t]hese results underscore the importance of confirming the function of newly identified gene products

even when database searches reveal significant homology to proteins of known function" (page 441, left-hand column).

Bork, Skolnick, *et al.* and Scott, *et al.* all agree that experimental confirmation of data, *e.g.*, amino acid sequence alignments, gathered through computational methods is a necessity and sole reliance on sequence alignment data may lead to incorrect hypotheses.

The current specification teaches that *coaX* is a second, novel pantothenate kinase gene that was initially identified through sequence analysis and ultimately verified to function as a pantothenate kinase gene based on a functional assay, *e.g.*, ability to complement the *E. coli* temperature sensitive *coaA* mutation. As stated by the Examiner, the specification is clearly enabled for methods to experimentally determine the biochemical function of a protein, *e.g.*, a protein with pantothenate kinase activity and therefore have provided sufficient guidance such that one skilled in the art can identify any or all such proteins with pantothenate kinase activity without undue experimentation. Applicants are also very much aware of the need for functional assays to confirm computational results as well as the plethora of errors that exist in public sequence databases. Moreover, Applicants have demonstrated their ability to effectively utilize the methods described in the instant specification to perform sequence analysis and exploit genomic context as first steps, identify conserved amino acid residues, functionally confirm those results, and functionally identify errors within publicly available databases. See Example IV, page 37:

> Several homologues of the *B. subtilis coaX* gene were identified by homology searching of various publicly available databases using the published *yacB* (*coaX*) open reading frame sequence and predicted amino acid sequence (as set forth in SEQ ID NOs:15 and 16 respectively). In two cases *(Mycobacterium tuberculosis and Streptomyces coelicolor)* ***the homologous coaX genes are adjacent to, or almost adjacent to, pantothenate biosynthetic genes, consistent with these homologs having a role in pantothenate metabolism.*** The CoaX proteins show no homology to the CoaA family of pantothenate kinases, nor to the eukaryotic family of pantothenate kinases exemplified by PanK of *Saccharomyces cerevisiae.*
>
> Alignment of the amino acid sequences of several bacterial CoaX homologs with the amino acid sequence predicted from translating the *B. subtilis yacB* ORF described in the published *B. subtilis* genome sequence revealed that the CoaX

proteins from other bacteria contained additional amino acid residues at their carboxy-terminal ends. Moreover, these extensions beyond the end of the predicted amino acid sequence for the *B. subtilis* gene product contained two relatively well conserved segments of sequence.

Translation of nucleotide sequences just downstream from the stop codon of the *B. subtilis yacB* ORF in a different reading frame revealed the existence of amino acid sequences very similar to the carboxy-terminal extensions of the other bacterial CoaX proteins. ***It is thus believed that an error exists in the published DNA sequence of the B. subtilis yacB ORF sequence that causes a frame shift leading to an artifactual downstream amino acid sequence and premature termination.***

In view of the foregoing comments, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-14 under 35 USC §112, first paragraph.

Claims 1-14 and 37 are rejected under 35 USC §112, first paragraph, as failing to comply with the written description requirement. The Examiner states that the applicant has "not demonstrated that all of the proteins so identified are actually members of the claimed genus" and that no "structural feature that identifies a CoaX protein, other than that those proteins are encoded by genes that are structurally distinct from other panthothenate kinase genes" have been provided in the specification.

Applicants respectfully traverse. Applicants have provided not only the structural basis for the claimed genus, *e.g.*, that they are distinct from CoaA proteins as well as the conserved amino acid residues depicted in Figure 6 (see below), but they have also provided a functional basis for the claimed genus, *e.g.*, complementation of the temperature sensitive CoaA in *E. coli* YH1. Figure 6 identifies amino acid residues that are conserved in all of the protein sequences aligned by the ClustalW method. For example, in Figure 6B, the "*" underneath the glycine as well as underneath the aspartic acid of the alignment indicate that at those positions in each of the proteins aligned there is always a glycine or an aspartic acid. Figure 6 identifies numerous amino acids that are 100% conserved in each of the proteins aligned, *e.g.*, all of the residues identified with an "*". Figure 6 also identifies numerous residues that are conserved in the sense that the majority of the proteins contain an identical residue, however in some of the proteins there is a conservative amino acid substitution. For example, Figure 6C identifies an

isoleucine residue with an ":" in *B. subtilis*. Looking down the column, all of the proteins at that position contain an isoleucine, a leucine or a valine; all amino acids of the same family, *e.g.*, those with nonpolar side chains. Similarly, the threonine residue in the *B. subtilis* protein with an ":" is conserved in all of the proteins except for *M. tuberculosis* and *H. pylori* in which a serine has been substituted for a threonine. Numerous additional examples are shown in Figure 6. The combination of the protein analysis and the experimental analysis of the present invention clearly provide sufficient written description for one skilled in the art to identify CoaX proteins.

In view of the foregoing comments, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-14 and 37 under 35 USC §112, first paragraph.

Rejection of Claims 1-14 and 37 Under 35 USC §112, Second Paragraph

Claims 1-14 and 37 are rejected under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner states that the "specification provides a sequence alignment of a number of proteins, but does not identify any regions or motifs that are essential to the protein function, or that identify a particular pantothenate kinase as a CoaX protein". "in view of the lack of a identified structure by which one skilled in the art could identify a member of this group and the lack of correlation between the protein family's assigned function and such a structure, one skilled in the art would not, from the present disclosure, be able to determine if a particular protein with a pantiothenate kinase activity was, or was not a member of the CoaX protein genus".

Applicants respectfully traverse and reiterate that they have provided not only the structural basis for the claimed genus, *e.g.*, that they are distinct from CoaA proteins as well as the conserved amino acid residues depicted in Figure 6, but they have also provided a functional basis for the claimed genus, *e.g.*, complementation of the temperature sensitive CoaA in *E. coli* YH1. As discussed above, Applicants have shown multiple amino acid residues in Figure 6 that

are conserved among the aligned proteins. Applicants have also provided numerous working examples of the invention that allow one skilled in the art to experimental define a CoaX protein. The conserved amino acids identified in Figure 6 will allow one to tentatively identify a novel amino acid sequence as a member of the CoaX protein and the methods of the invention provide significant guidance to one skilled in the art to experimentally assign a pantothenate kinase function to the protein under examination.

In view of the foregoing comments, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-14 and 37 under 35 USC §112, second paragraph.

Rejection of Claim 37 Under 35 USC §102(e)

Claim 37 is rejected under 35 USC §102(e) as being anticipated by Dougherty, *et al.* The Examiner states that Dougherty, *et al.* "teaches the identification of antibacterial compounds by identifying compounds that disrupt the function of a class of bacterial proteins identified as conserved essential gene (CEG) proteins". "Among the proteins identified as CEG proteins is pantothenate kinase. Page 41. Thus, the reference teaches the identification of antibacterial compounds (antibiotics) by identifying compounds that disrupt (modulate) pantothenate kinase activity. The reference therefore anticipates the identified claims".

Applicants respectfully traverse and submit that Dougherty, *et al.* teach that the disruption of a sequence that encodes a gene with pantothenate kinase activity in *Streptococcus pneumoniae* is lethal. The current specification, however, teaches that, surprisingly, organisms such as *Bacillus subtilis* contain a second gene responsible for pantothenate kinase activity, the *coaX* gene. Furthermore, the present specification teaches that this gene, *coaX,* contains no sequence homology to the *coaA* gene and that only disruption of both *coaA* and *coaX* genes is lethal to the organism. Therefore, based on the teachings of Dougherty, *et al.* who teach that a conserved essential gene, *e.g., coaA*, is a ***gene or gene product whose function is required for***

cell viability, *e.g.* lethal if absent, it would not be expected that disruption of the pantothenate kinase gene, *coaA*, would permit the cells to survive as demonstrated in Example V, page 38:

> ...deletion of *coaX* by itself is not lethal for *B. subtilis*. Furthermore, chromosomal DNA from PA876 would not transform competent PA861 (PY79 Δ*coaA* ::*cat*) to kanamycin resistance. These results indicate that it is the combination of Δ*coaA*::*cat* and Δ*coaX* :: *kan* that is lethal for *B. subtilis*...

In view of the foregoing comments, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 37 under 35 USC §102(e).

The Examiner has made the following three prior art references of record and stated that they are not the basis for rejection of the claims for stated reasons.

U.S. Patent Application Publication 2002/0160456, Kleanthous, *et al.,* teaches use of proteins from *Heliobacter* as potential vaccines against *Heliobacter* infections. Among the proteins is SEQ ID NO:74 which is 100% identical to SEQ ID NO:14 and SEQ ID NO:67 in the present application. However, Kleanthous, *et al.* does not teach the function of the protein or its use to identify antibiotics.

U.S. Patent Application Publication 2002/0164588, Eisenberg, *et al.,* teaches a method to identify bacterial genes and proteins as potential targets of anti-bacterial drugs. One of the proteins identified in this reference is SEQ ID NO:74 which shares 99.7% homology with SEQ ID NO: 5 of the present specification. Eisenberg, *et al.,* do not teach the use of this protein as a drug target or identify the function of this protein.

DeShazer, *et al.* teach that the *B. pertussis* baf protein is an essential protein and therefore may be an antibacterial drug target. The *B. pertussis* baf protein is identical to SEQ ID NO:15 of the present specification. Nevertheless, DeShazer, *et al.* do not teach the function of the protein or methods to identify compounds that inhibit pantothenate kinase activity.

Applicants concur with the Examiner's evaluation of these three references and agree that they do not teach the methods of the present invention for the above stated reasons.

CONCLUSION

In view of the above amendments and remarks, it is believed that this application is in condition for allowance. If a telephone conversation with Applicants' Attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Date: December 2, 2003

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By ______________________

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Appendix

FIG. 6A

CLUSTAL W (1.7) Multiple Sequence Alignments

Sequence type explicity set to Protein
Sequnce format is Pearson

~~Seq. 1:~~ B. subtilis |CoaX ~~| SEQNO_9~~ 258 aa
~~Seq. 2:~~ dbj | BAA21476.1 | D. vulgaris 212 aa
~~Seq. 3:~~ gb | AAD35964.1 | T. maritima 246 aa
~~Seq. 4:~~ pir | T36391 | S. coelicolor 265 aa
~~Seq. 5:~~ sp | Q45338 | B. pertussis 267 aa

~~Seq. 6:~~ sp | O06282 | M. tuberculosis 272 aa
250aa
~~Seq. 7:~~ gb | O93446 | T. pallidum 273 aa

~~Seq. 8:~~ sp | O51477 | B. burgdorferi 262 aa
~~Seq. 9:~~ sp | P74045 | Synechocystis 257 aa
~~Seq. 10:~~ sp | O25533 | H. pylori 223 aa
~~Seq. 11:~~ sp | O67753 | A. aeolicus 229 aa
~~Seq. 12:~~ sp | Q9RX54 | D. radiodurans 262 aa

~~Seq. 13:~~ WIT | RCA03301| C. acetobutylicum

~~Seq. 14:~~ WIT | RRC02473 | R. capsulatus 258 aa

B. subtilis |CoaX ~~| SEQIDNO_9~~ -----------------MLLVIDVGNTNTVLGVYHDG----KLEYHWRIE
WIT | RCA03301| C. acetobutylicum NKRAAFMLLLFLRSVLKVILVLDVGNTNIVLGIYNDT----KLTAEWRLS
pir | T36391 | S. coelicolor -----------------MLLTIDVGNTHTVLGLFDGE----DIVEHWRIS
sp | O06282 | M. tuberculosis -----------------MLLAIDVRNTHTVVGLLSGMKEHAKVVQQWRIR
WIT | RRC02473 | R. capsulatus -----------------MLLCIDCGNTNTVFSVWDGT----DFAATWRIA
dbj | BAA21476.1 | D. vulgaris --------------MTQHFLLFDIGNTNVKIGIAVET----AVLTSYVLP
sp |Q9RX54 |D. radiodurans -------------MPAFPLLAVDIGNTTTVLGLADASG---ALTHTWRIR
gb | AAD35964.1 | T. maritima -----------------MYLLVDVGNTHSVFSITEDG----KTFRRWRLS
gb | O93446 | T. pallidum ------------------MLLIDVGNSHVVFGIQGENGGRVCVRELFRLA
sp | O51477 | B. burgdorferi -----------MNKPLLSELIIDIGNTSIAFALFKDN----QVNLFIKMK
sp | O67753 | A. aeolicus ----------------MRFLTVDVGNSSVDIALWEGK----------KVK
sp | P74045 | Synechocystis ----------METSKPGCGLALDNDKQKPWLGLMIGN-----SRLHWAYC
sp | O25533 | H. pylori --------------MPARQSFTDLKN---LVLCDIGN-----------TR
sp | Q45338 | B. pertussis -----------------MIILIDSGNSRLKVGWFDPDAP--QAAREPAPV

FIG. 6B

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B. subtilis |CoaX | SEQIDNO_9                TSRHKTEDEFGMILRSLFDHS----GLMFEQIDGIIISSVVPPIMFALER
WIT | RCA03301| C. acetobutylicum           TDVLRSADEYGIQVMNLFQQD----KLDPTLVEGVIISSVVPNIMYSLEH
pir | T36391 | S. coelicolor                TDSRRTADELAVLLQGLMGMHPLLGDELGDGIDGIAICATVPSVLHELRE
sp | O06282 | M. tuberculosis               TESEVTADELALTIDGLIG-------EDSERLTGTAALSTVPSVLHEVRI
WIT | RRC02473 | R. CAPSULATUS              TDHRRTADEYFVWLNTLMQLK-----GLQGRISEAIISSTAPRVVFNLRV
dbj | BAA21476.1 | D. vulgaris              TDPGQTTDSIGLRLLEVLRHAG----LGPADVGACVASSVVPGVNPLIRR
sp |Q9RX54 |D. radio radiodurans               TNREMLPDDLALQLHGLFTLA-----GAP-IPRAAVLSSVAPPVGENYAL
gb | AAD35964.1 | T. maritima              TGVFQTEDELFSHLHPLLG-------DAMREIKGIGVASVVPTQNTVIER
gb | O93446 | T. pallidum                   PDARKTQDEYSLLIHALCERAG----VGRASLRDAFISSVVPVLTKTIAD
sp | O51477 | B. burgdorferi                TNLMLRYDEVYSFFEENFDFN------VN---K-VFISSVVPILNETFKN
sp | O67753 | A. aeolicus                   DFLKLSHEEFLKEEFPKLK---------------ALGISVKQSFSEKVRG
sp | P74045 | Synechocystis                 SGNAPLQTWVTDYNPKSAQLP-------------VLLGKVPLMLASVVPE
sp | O25533 | H. pylori                     IHFAQNYQLFSSAKEDLKR---------------LGIQKEIFYISVNEE
sp | Q45338 | B. pertussis                  AFDNLDLDALGRWLATLPRRP-------Q----RALGVNVAGLARGEAIA

B. subtilis |CoaX | SEQIDNO_9                MCTKYFHIEPQIVG-PG-MKTGLNIKYDNPKEVGADRIVNAVAAIHLYG-
WIT | RCA03301| C. acetobutylicum           MIRKYFKINPLVVG-PG-IKTGINIKYDNPKEVGADRIVNAVAAHEIYK-
pir | T36391 | S. coelicolor                VTRRYYGDVPAVLVEPG-VKTGVPILTDHPKEVGADRIINAVAAVELYG-
sp | O06282 | M. tuberculosis               MLDQYWPSVPHVLIEPG-VRTGIPLLVDNPKEVGADRIVNCLAAYDRFR-
WIT | RRC02473 | R. capsulatus              LCNRYFDCRPYVVGKPG-CELPVAPRVDPGTTVGPDRLVNTVAGYDRHG-
dbj | BAA21476.1 | D. vulgaris              ACERYL--YRKLLFAPGDIAIPLDNRYERPAEVGADRLVAAYAARRLYP-
sp |Q9RX54 |D. radiodurans                  ALKRHFMIDAFAVSAEN-LPDVTVELDTPGSVGADRLCNLFGAEKYLG-
gb | AAD35964.1 | T. maritima              FSQKYFHISPIWVKAKN---GCVKWNVKNPSEVGADRVANVVAFVKEYG-
gb | O93446 | T. pallidum                   AVAQISGVQPVVFGPWAYEHLPVRIPEPVRAEIGTDLVANAVAAYVHFR-
sp | O51477 | B. burgdorferi                VIFSFFKIKPLFIGFDLNYDLTFNPYKSDKFLLGSDVFANLVAAIENYS-
sp | O67753 | A. aeolicus                   KIPKIK-----FLKKEN---FPIQVDYKTPETLGTDRVALAYSAKKFYG-
sp | P74045 | Synechocystis                 QTEVWRVYQPKILTLKN---LPLVNLYP---SFGIDRALAGLGTGLTYG-
sp | O25533 | H. pylori                     NEKALLNCYPNAKNIAG--FFHLETDYVG---LGIDRQMACLA---VN--
sp | Q45338 | B. pertussis                  ATLRAGGCDIRWLRAQP-LAMGLRNGYRNPDQLGADRWACMVGVLARQPS
                                                       .               .* *        .
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FIG. 6C

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B. subtilis |CoaX | SEQIDNO_9                NP--LIVVDFGTATTYCYIDENKQYMGGAIAPGITISTEALYSRAAKLPR
WIT | RCA03301| C. acetobutylicum           RS--LIIIDFGTATTFCAVRENGDYLGGAICPGIKVSSEALFEKAAKLPR
pir | T36391 | S. coelicolor                GP--AIVVDFGTATTFDAVSARGEYIGGVIAPGIEISVEALGVKGAQLRK
sp | O06282 | M. tuberculosis               KA--AIVVDFGSSICVDVVSAKGEFLGGAIAPGVQVSSDAAAARSAALRR
WIT | RRC02473 | R. capsulatus             GD--LIVVDFGTATTFDVVAPDGAYIGGVIAPGVNLSLEALHMAAAALPH
dbj | BAA21476.1 | D. vulgaris             GPRSLVSVDFGTATTFDCVEG-GAYLGGLICPGVLSSAGALSSRTAKLPR
sp |Q9RX54 |D. radiodurans                 GLDYAVVVDFGTSTNFDVVGRGRRFLGGILATGAQVSADALFARAAKLPR
gb | AAD35964.1 | T. maritima             KN--GIIIDMGTATTVDLVVN-GSYEGGAILPGFFMMVHSLFRGTAKLPL
gb | O93446 | T. pallidum                  SA--CVVVDCGTALTFTAVDGTGLIQGVAIAPGLRTAVQSLHTGTAQLPL
sp | O51477 | B. burgdorferi               FEN-VLVVDLGTACTIFAVSRQDGILGGIINSGPLINFNSLLDNAYLIKK
sp | O67753 | A. aeolicus                  KN--VVVISAGTALVIDLVLE-GKFKGGFITLGLGKKLKILSDLAEGIPE
sp | P74045 | Synechocystis                FP--CLVVDGGTALTITGFDQDKKLVGGAILPGLGLQLATLGDRLAALPK
sp | O25533 | H. pylori                    NG---VVVDAGSAITIDLIKE-GKHLGGCILPGLAQYIHAYKKSAKILEQ
sp | Q45338 | B. pertussis                 VHPPLLVASFGTATTLDTIGPDNVFPGGLILPGPAMMRGALAYGTAHLPL
                                                  :  . *::     .       *  :  *              :

B. subtilis |CoaX | SEQIDNO_9                IEITRPDN---IIGKNTVSAMQSGILFGYVGQVEGIVKRMKWQAKQDLK-
WIT | RCA03301| C. acetobutylicum           VELIKPAY---AICKNTISSIQSGIVYRYLRQVKYLFEKLKENLPDGRRT
pir | T36391 | S. coelicolor                IEVARPRS---VIGKNTVEAMQSGIVYGFAGQVDGVVNRMARELADD--P
sp | O06282 | M. tuberculosis               VELARPRS---VVGKNTVECMQAGAVFGFAGLVDGLVGRIREDVSGFSVD
WIT | RRC02473 | R. capsulatus             VDVTKPQG---VIGTNTVACIQSGVYWGYIGLVEGIVRQIRMERDRP---
dbj | BAA21476.1 | D. vulgaris             ISLEVEEDS-PVIGRSTTTSLNHGFIFGFAAMTEGVLAA-----------
sp |Q9RX54 |D. radiodurans                 ITLQAPET---AIGKNTVHALQSGLVFGYAEMVDGLLRRIRAELPGE---
gb | AAD35964.1 | T. maritima             VEVKPADF---VVGKDTEENIRLGVVNGSVYALEGIIGRIKEVYGDLP--
gb | O93446 | T. pallidum                  VPLALPDS---VLGKDTTHAVQAGVVRGTLFVIRAMIAQCQKELGCR---
sp | O51477 | B. burgdorferi               FPISTPNN---LLERTTSGSVNSGLFYQYKYLIEGVYRDIKQMYKKK---
sp | O67753 | A. aeolicus                  FFPEEVEI---FLGRSTRECVLGGAYRESTEFIKSTLKLWRKVFKRK---
sp | P74045 | Synechocystis                LEMDQLTELPDRWALDTPSAIFSGVVYGVLGALQSYLQDWQKLFPGA---
sp | O25533 | H. pylori                    PFKALDSL--EVLPKSTRDAVNYGMVLSVIACIQHLAK--NQK-------
sp | Q45338 | B. pertussis                 ADGLVADY-----PIDTHQAIASGIAAAQAGAIVRQWLAGRQRYGQAP--
                                                             *   :  *
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FIG. 6D

B. subtilis |CoaX | ~~SEQIDNO_9~~	----VIATGG--------LAPLIANES-----DCIDIVDPFLTLKGLELI
WIT | RCA03301| C. acetobutylicum	RTSLVLATGG--------LAKLIN-------------------------
pir | T36391 | S. coelicolor	DDVTVIATGG--------LAPMVLGES-----SVIDEHEPWLTLMGLRLV
sp | O06282 | M. tuberculosis	HDVAIVATGH--------TAPLLLPEL-----HTVDHYDQHLTLQGLRLV
WIT | RRC02473 | R. capsulatus	--MKVIATGG--------LASLFDLGF-----DLFDKVEDDLTMHGLRLI
dbj | BAA21476.1 | D. vulgaris	--
sp |Q9RX54 |D. radiodurans	--AVAVATGG--------FSRTVQGIC-----QEIDYYDETLTLRGLVEL
gb | AAD35964.1 | T. maritima	----VVLTGG--------QSKIVK-DM-----IKHEIFDEDLTIKGVYHF
gb | O93446 | T. pallidum	--CAAVITGG--------LSRLFS-SE-----VDFPPIDAQLTLSGLAHI
sp | O51477 | B. burgdorferi	--FNLIITGG--------NADLILSLI-----EIEFIFNIHLTVEGVRIL
sp | O67753 | A. aeolicus	--FKVVITGG--------EGKYFS---------KFGIYDPLLVHRGMRNL
sp | P74045 | Synechocystis	---AMVITGG--------DGKILHGFLKEHSPNLSVAWDDNLIFLGMAAI
sp | O25533 | H. pylori	----IYLCGG--------DAKYLSAFL------PHSVCKERLVFDGMEIA
sp | Q45338 | B. pertussis	---EIYVAGGGWPEVRQEAERLLAVTGAAFGATPQPTYLDSPVLDGLAAL

B. subtilis |CoaX | ~~SEQIDNO_9~~	YERNRVGSV----------
WIT | RCA03301| C. acetobutylicum	-------------------
pir | T36391 | S. coelicolor	YERNVSRM-----------
sp | O06282 | M. tuberculosis	FERNLEVQRGRLKTAR---
WIT | RRC02473 | R. capsulatus	FDYNKGLGA----------
dbj | BAA21476.1 | D. vulgaris	-------------------
sp |Q9RX54 |D. radiodurans	WASRSEVR-----------
gb | AAD35964.1 | T. maritima	CFGD---------------
gb | O93446 | T. pallidum	ARLVPTSLLPPATVSGSSGN
sp | O51477 | B. burgdorferi	GNSIDFKFVN---------
sp | O67753 | A. aeolicus	LYLYHRI------------
sp | P74045 | Synechocystis	HHGDRPIC-----------
sp | O25533 | H. pylori	LKKAGILECK---------
sp | Q45338 | B. pertussis	AAQGAPTA-----------